IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Yi Wang

Serial No. 10/655,861 Confirmation No.: 7250

Filed: 5 September 2003 Examiner: F. P. VanderVegt

FOR: METHOD OF TREATMENT OF ASTHMA USING ANTIBODIES TO COMPLEMENT COMPONENT C5 Group Art Unit: 1644

DECLARATION UNDER 37 CFR § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Dr. Rick A. Wetsel, declare as follows:

1. I am the senior author of the publication "Expression of the Complement Anaphylatoxin C3a and C5a Receptors on Bronchial Epithelial and Smooth Muscle Cells in Models of Sepsis and Asthma" published by Drouin et al. in the *Journal of Immunology* 166:2025-2032 (2001).

2. I received a B.S. in Chemistry in 1976 from the University of Texas at Austin, a Ph.D. in Biochemistry in 1982 from the University of Texas Health Science Center at San Antonio, and I performed postdoctoral training in Immunology from 1983-1986 at the Scripps Research Institute, La Jolla, California. From 1986-1996 I was an Assistant Professor of Pediatrics and Assistant Professor of Molecular Microbiology, Washington University School of Medicine, Department of Pediatrics, St. Louis, Missouri. In 1992 I was a Visiting Investigator, Basel Institute for Immunology, Basel, Switzerland. From 1996-2001 I was an Associate Professor, Research Center for Immunology and Autoimmune Diseases, Institute of Molecular Medicine for the Prevention of Human Diseases, University of Texas-Houston, Houston, Texas; Director, Laboratory for Developmental Biology. From 2001-Present I have been Professor, Research Center for Immunology and Autoimmune Diseases, Institute of Molecular Medicine for the Prevention of Human Diseases, University of Texas-Houston; Director, Laboratory for Developmental Biology.

3. Alexion Pharmaceuticals, Inc., the Assignee of U.S. Patent Application Serial No. 10/655,861 entitled "Method of Treatment of Asthma Using Antibodies to Complement Component C5" has asked me to clarify the intended meaning of some statements in the Drouin et al. publication cited above for which I am the senior author. Specifically, the statements in the

first paragraph of the Discussion section on page 2029 may have been written less precisely than we intended, and this has apparently led to a conflict in the way that Alexion Pharmaceuticals interprets the statements as compared to the way the U.S. Patent and Trademark Office has interpreted the statements. Our intended meaning of the statements at issue is as follows.

4. The results disclosed in the Drouin et al. publication cited above show that C5aR is upregulated in the lung after LPS treatment; however, in the OVA model of allergic lung disease the C5aR was **not** upregulated. Instead, in the OVA model only the C3aR showed increased expression. Furthermore, C3aR is upregulated in the OVA model only on the smooth muscle cells.

5. The first paragraph of the Discussion on page 2029 of the cited Drouin et al. publication states, "This study documents for the first time the expression of C3aR by lung cells and confirms previous reports that cells endogenous to mouse and human lungs express C5aR. Moreover, we have established that both receptors are up-regulated in two distinct models of lung inflammation: endotoxemia and OVA-induced asthma." This opening sentence of the discussion was meant to be only general, with the more detailed differences discussed on pages 2030 and 2031. Since this opening sentence has caused some confusion, I wish we had written it in a more precise manner. In any event, on page 2031 we state the details: "In contrast to mice treated with LPS, C3aR and C5aR expression did not change on bronchial and alveolar epithelial cells from OVA-challenged lungs. However, bronchial smooth muscle expression of C3aR was increased in OVA-challenged mice relative to the saline controls."

6. The disagreement between Alexion Pharmaceuticals and the U.S. Patent and Trademark Office appears to be that concerning the language "Moreover, we have established that both receptors are up-regulated in two distinct models of lung inflammation: endotoxemia and OVA-induced asthma". One party's interpretation is that 1) C3aR and C5aR are both upregulated in both endotoxemia and OVA-induced asthma; whereas the second party interprets the language as 2) C3aR and C5aR are both upregulated in endotoxemia whereas only C3aR is upregulated in the OVA-induced asthma model. The second interpretation is correct. Only C3aR is upregulated in the OVA-induced asthma model and to be precise it was only the C3aR on bronchial smooth muscle that was increased in the OVA model. C5aR was not shown to be upregulated in the OVA-induced asthma model in the data presented in the above-cited Drouin et al. publication.

I further state that the above statements were made with the knowledge that willful false statements and the like are punishable by fine and/or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that any such willful false statement may jeopardize the validity of this application or any patent resulting therefrom.

Dated: May 21, 2009

Rick A. Wetsel

Rick A. Wetsel, Ph.D.